



This document is scheduled to be published in the Federal Register on 04/24/2014 and available online at <http://federalregister.gov/a/2014-09354>, and on FDsys.gov

[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S.

Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 209 and 37 CFR Part 404 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Use of Antihistamine Compounds for the Treatment of Hepatitis C Virus

Description of Technology: The vast majority of people infected with Hepatitis C Virus (HCV) will have chronic infection. Over decades, this can lead to liver disease and liver cancer. In fact, HCV infection is the leading cause of liver transplants in the U.S. Several new drugs have recently come into the market that will likely change the HCV treatment paradigm. However, the effectiveness of these new drugs can vary depending on the HCV genotype. Thus, there is still the need for additional new therapeutics against HCV.

The subject technology are small molecule compounds identified using a novel cell-based high throughput assay of HCV infection. The compounds are antihistamines that show potent antiviral properties against HCV. One advantage of these compounds is that they are already on the market for the treatment of allergic reactions and, thus, have been used extensively in humans and have excellent safety profiles with known pharmaceutical properties. The subject technology can also potentially be used in combination with other HCV therapeutics.

Potential Commercial Applications: Prevention or treatment of HCV infection.

Competitive Advantages: These compounds are already on the market and, thus, have known safety profiles and pharmaceutical properties.

Development Stage:

- Early-stage
- In vitro data available

Inventors: Jake Tsanyang Liang (NIDDK), Juan Jose Marugan (NCATS), Noel Terrance Southhall (NCATS), Xin Hu (NCATS), Jingbo Xiao (NCATS), Shanshan He (NIDDK), Marc Ferrer (NCATS), Zongyi Hu (NIDDK), Wei Zhang (NCATS)

Intellectual Property: HHS Reference No. E-011-2014/0 – US Provisional Patent Application No. 61/909,414 filed 27 Nov 2013

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018;
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Intranasal Nebulizer with Disposable Drug Cartridge for Improved Delivery of Vaccines and Therapeutics

Description of Technology: Intranasal delivery is a simple, inexpensive and needle-free route for administration of vaccines and therapeutics. This intranasal delivery technology, developed with Creare LLC, includes low-cost, disposable drug cartridges (DDCs) that mate with a durable hand-held device. The rechargeable-battery-powered device transmits ultrasonic energy to the DDC to aerosolize the drug and is capable of performing for eight hours at 120 vaccinations per hour. Potential applications for this platform technology include intranasal vaccination (e.g. seasonal or pandemic influenza vaccines) and intranasal delivery of locally active (e.g. antihistamines, steroids) or systemically active (e.g. pain medications, sedatives) pharmaceuticals.

The DDCs themselves offer two unique benefits. First, all components that contact the active agent or the patient may be easily disposed of, which reduces the risk of patient cross-contamination and minimizes cleaning and maintenance requirements of

the hand-held device. Second, DDCs provide a low-cost and simple method to package and distribute individual doses.

This technology also allows for significant dose-sparing. Preliminary studies have shown robust immune responses when this technology is used to delivery significantly reduced doses of Live Attenuated Influenza Vaccine in animal models. The intranasal nebulizer produces droplets sized for optimum depositioning in the nasal airway. The small nebulizer droplets essentially “spray paint” the internal nasal airway, resulting in an increased tissue surface coverage that may enable a significant dose reduction. In contrast, currently available nasal delivery devices, such as nasal sprays and droppers, do not provide efficient intranasal delivery in humans because the large droplets they generate fail to coat a significant portion of the nasal airway. Large droplets also tend to drip out of the nose or down the throat, which can be unpleasant for the patient in addition to wasting a sizable portion of the active agent.

Potential Commercial Applications:

- Intranasal delivery of vaccines and therapeutics
- Childhood vaccination programs, mass immunization campaigns, or response to epidemics

Competitive Advantages:

- Safe, needle-less delivery
- No patient-to-patient contamination
- Long-life, rechargeable battery
- Consistent delivery and dose-sparing

- Nasal delivery of live-attenuated vaccines may be more effective than traditional injected vaccines

- Cost-effective
- Reduces biohazard waste
- May be administered by personnel with minimal medical training
- Easy means of delivery to children with fear of needles

Development Stage:

- Prototype
- In vitro data available
- In vivo data available (animal)

Inventors: Mark J. Papania (CDC), et al.

Publication: Smith JH, et al. Nebulized live-attenuated influenza vaccine provides protection in ferrets at a reduced dose. *Vaccine*. 2012 Apr 19;30(19):3026-33. [PMID 22075083]

Intellectual Property:

- HHS Reference No. E-308-2013/0 –
 - PCT Application No. PCT/US2011/039020 filed on 03 Jun 2011, which published as WO 2011/153406 on 08 Dec 2011
 - US Patent Application No. 13/701,992 filed 04 Dec 2012
 - Various international pending patents
- HHS Reference No. E-323-2013/0 –
 - PCT Application No. PCT/US2002/007973 filed 13 Mar 2002, which published as WO 2002/074372 on 26 Sep 2002

- US Patent No. 7,225,807 issued 05 Jun 2007
- US Patent No. 8,544,462 issued 01 Oct 2013
- Various international issued patents
- HHS Reference No. E-324-2013/0 –
 - PCT Application No. PCT/US2005/011086 filed 01 Apr 2005, which published as WO 2006/006963 on 19 Jan 2006
 - US Patent No. 7,954,486 issued 07 Jun 2011
 - US Patent No. 8,656,908 issued 25 Feb 2014
 - Various international issued patents
- HHS Reference No. E-564-2013/0 - US Provisional Application No. 61/808,547 filed 04 Apr 2013

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Silica Exposure Safety: Mini-baghouse Systems and Methods for Controlling Particulate Release from Large Sand Transfer Equipment

Description of Technology: CDC/NIOSH scientists have developed an effective point-source control for silica-containing dusts that can be generated from machinery on sites where hydraulic fracturing is occurring. The CDC/NIOSH mini-baghouse retrofit assembly is a bolt-on control designed to contain silica-containing respirable dusts generated during refill operations of sand movers during hydraulic fracturing.

In the U.S., most new oil and gas wells are hydraulically fractured to enhance well production. Most hydraulic fracturing operations have 2-5 sand movers on-site

which transfer thousands to millions of pounds of silica sand during each stage of fracturing. While a variety of passive and active controls are currently available (or have been proposed) to limit release of silica-containing dusts, the CDC/NIOSH mini-baghouse retrofit assembly was designed to fill a unique need for a control. The retrofit to equipment can be made in the field, uses existing energy inherent in the system and is relatively simple and effective. CDC/NIOSH field research has shown that risks for exposure to respirable silica arise from at least 8 points of dust generation and that a variety of controls (engineering, administrative and personal protective equipment) are needed to control exposures. Use of the mini-baghouse retrofit technology is intended to limit release of respirable silica from thief hatches on top of the sand movers, enhancing workplace health and safety.

Potential Commercial Applications:

- Controlling occupational exposure to respirable crystalline silica, particularly during work involving transfer of sand into sand movers on hydraulic fracturing sites
- In-field retrofits of currently operating heavy equipment (e.g., sand movers)
- Limiting visible dust emissions from sand moving equipment
- Reducing respirable crystalline silica dust emissions to enhance compliance with OSHA PEL for silica

Competitive Advantages:

- Designed for in-field retrofitting “thief hatches” of existing machinery
- Uses energy inherent in the pneumatic transfer of sand
- Provides a passive sand-mover-mounted control for silica release at hydraulic fracturing operations

Development Stage:

- In situ data available (on-site)
- Prototype

Inventors: Eric J. Esswein, Michael Breitenstein, John E. Snawder, Michael G. Gressel, Jerry L. Kratzer (all of CDC)

Publication: Esswein EJ, et al. Occupational exposures to respirable crystalline silica during hydraulic fracturing. *J Occup Environ Hyg.* 2013;10(7):347-56. [PMID 23679563]

Intellectual Property: HHS Reference No. E-291-2013/0 – US Application No. 13/802,265 filed 13 Mar 2013

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Viral Like Particles Based Chikungunya Vaccines

Description of Technology: Chikungunya virus (CHIKV) is mosquito-borne alphavirus endemic in Africa, India, and Southeast Asia. In 2013 CHIKV infection has also emerged in the Caribbean and a pandemic of CHIKV has re-emerged in the Philippines following Typhoon Haiyan. Currently, there is no vaccine available for the prevention of CHIKV infection and no specific therapy exists to treat the illness.

Researchers at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID) have developed a CHIKV Viral Like Particle (CHIKV VLP) vaccine based on plasmid expression vectors encoding structural proteins of the CHIKV virus, which gave rise to CHIKV VLPs in transfected cells. The CHIKV VLPs

consist of the core, E1 and E2 proteins and are similar in buoyant density and morphology to replication-competent CHIKV virus. Immunization with CHIKV VLPs elicited neutralizing antibodies against envelope proteins from different CHIKV strains in mouse and nonhuman primate (NHP) models. Monkeys immunized with CHIKV VLPs produced high titer neutralizing antibodies that protected against viremia after high dose challenge. The selected CHIKV VLP vaccine candidate, VRC-CHKVLP059-00-VP, composed of the E1, E2, and capsid proteins from the CHIKV strain 37997, was recently evaluated by the VRC at the NIH Clinical Center for safety, tolerability and immunogenicity in the clinical protocol VRC 311 (ClinicalTrials.gov # NCT01489358), a Phase I, open-label, dose escalation clinical trial. The VRC-CHKVLP059-00-VP vaccine was highly immunogenic, safe, and well-tolerated. VRC researchers have also developed the transient transfection manufacturing process for CHIKV and other alphaviruses, such as Western, Eastern and Venezuelan Equine Encephalitis (WEVEE) viruses. Pre-clinical in vivo mouse and NHP data, Phase 1 clinical trial data and manufacturing data are available.

Potential Commercial Applications: Chikungunya vaccines based on viral like particles.

Competitive Advantages:

- There is currently no CHIKV vaccine on the market.
- VRC-CHKVLP059-00-VP vaccine candidate is highly immunogenic, safe, and well-tolerated.
- Minimal containment requirements for CHIKV VLP manufacturing because live virus production is not required.

Development Stage:

- In vitro data available
- In vivo data available (animal)
- In vivo data available (human)

Inventors: Gary J. Nabel, Wataru Akahata, Srinivas S. Rao (all of VRC/NIAID)

Publications:

1. Akahata W, et al. A virus-like particle vaccine for epidemic Chikungunya virus protects non-human primates against infection. Nat Med. 2010 Mar;16(3):334-8. [PMID 20111039]
2. Akahata W, Nabel GJ. A specific domain of the Chikungunya virus E2 protein regulates particle formation in human cells: implications for alphavirus vaccine design. J Virol. 2012 Aug;86(16):8879-83. [PMID 22647698]
3. Chang et al. Chikungunya Virus-Like Particle Vaccine Elicits Neutralizing Antibodies in Healthy Adults in a Phase I Clinical Trial; manuscript submitted.

Intellectual Property:

- HHS Reference Nos. E-004-2009/0 /1 /2 –
 - US Provisional Application No. 61/118,206 filed 26 Nov 2008
 - US Provisional Application No. 61/201,118 filed 05 Dec 2008
 - International Application No. PCT/US2009/006294 (WO 2010/062396) filed 24 Nov 2009
 - and corresponding filings in the US, Europe, China, Australia, Brazil, India, Malaysia, South Africa, Singapore, Indonesia, Philippines and Vietnam

- HHS Reference No. E-057-2011/0 /1 /2 –

- US Provisional Application No. 61/438,236 filed 31 Jan 2011

- International Application No. PCT/US2012/023361 (WO 2012/106356) filed

31 Jan 2012

- and corresponding filings in the US and India

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April 21, 2014

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[FR Doc. 2014-09354 Filed 04/23/2014 at 8:45 am; Publication Date: 04/24/2014]